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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,119	11/18/1999	PHILIPPE SAUER	P63712US0	4763

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EXAMINER

PRATS, FRANCISCO CHANDLER

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 05/06/2003

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/341,119

Applicant(s)

SAUER ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

The request filed on October 17, 2002, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/341,119 is acceptable and a CPA has been established. An action on the CPA follows.

The previously non-entered after-final amendment filed September 17, 2002, has now been entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 14-37 have been cancelled.

Claims 38-60 have been added.

Claims 38-60 are pending and are examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-60 are rejected under 35 U.S.C. 112, first paragraph. The specification enables separating plasmid DNA from RNA and linear DNA by preferentially binding plasmid DNA over RNA and linear DNA to a silica support in the presence of a

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solution comprising 4 M potassium thiocyanate, 0.6 M NaCl, 0.1 M glycine, and 30% ethanol at a pH of 11.25 to 12.0. The specification also enables separating plasmid DNA from RNA and linear DNA by preferentially binding plasmid DNA over RNA and linear DNA to a silica support in the presence of a solution comprising 8.8 M sodium thiocyanate, 0.6 M NaCl, 0.1 M glycine, and 30% ethanol at a pH of 9.2 to 11.1. However, the specification does not reasonably provide enablement for using any chaotropic agent at any pH over 8 to separate plasmid DNA from RNA and linear DNA, as currently encompassed by the claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Specifically, although it is an established practice, the art of purifying plasmid DNA by binding the plasmids to silica in the presence of a chaotropic agent is well known to be a highly unpredictable art. For example, Gautsch et al (U.S. Pat. 6,027,750) clearly demonstrate that using certain chaotropic agents at pH 8.0, one cannot even obtain plasmid binding to glass. See Table 2, at cols. 13 and 14. See also, Boom et al, at col. 14, Example A5. Thus, Gautsch and Boom clearly demonstrate that the simple practice of binding plasmid DNA to glass or silica in the presence of a chaotropic agent is

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in fact a fairly unpredictable art requiring significant experimentation as to the selection and concentration of chaotropic agent, as well as the determination of suitable pH.

The process claimed by applicant adds the additional requirement that the plasmid DNA must preferentially bind to the silica without RNA or linear DNA binding to the silica. As applicant's own examples demonstrate, this also requires significant experimentation. See specification at pages 21 and 22. Note specifically that applicant's own examples demonstrate that no binding of either plasmid or linear DNA occurs above pH 12 in the preferred binding solution, despite the fact that such a pH and solution is clearly encompassed by the current claim language. Thus, applicant's own example demonstrates that the claimed objective of preferential plasmid DNA binding cannot be achieved under all of the conditions encompassed by the claims.

Thus, with the exception of the conditions mentioned above, the artisan of ordinary skill clearly would expect to have to undertake a significant amount of experimentation to determine which of the many parameters currently encompassed by the claims is truly suitable for binding plasmid DNA in a manner such that it can be separated from RNA and linear DNA. Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary;

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limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-47 and 50-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "crude bacterial lysate" in claim 38 renders that claim and its dependents indefinite because it is not clear what level of purification of bacterial cells is required by the claim. This ground of rejection can be overcome by deleting the term "crude." Note, however, that such an amendment would leave the claims encompassing lysates subjected to a number of purification steps. Alternatively, in view of the fact that applicant's asserted distinction over the prior art is the lack of a requirement of initial purification steps, applicant could

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amend the claims to recite that the lysate is -- prepared by a process consisting of -- those steps applicant considers essential to the process. In this regard, note the suggested use of "consisting of" language, which would exclude any additional steps applicant would assert as being not required by the process.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38-42, 44-47, 50-53 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (U.S. Pat.

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5,075,430) and Marko et al (Anal. Biochem. 121(2):382-387 (1982)).

Each of Little and Marko disclose the preparation of plasmid DNA by binding the plasmid to silica or glass in the presence of a chaotropic agent at pH 8, and in the presence of non-plasmid DNA or RNA species. See, e.g., Little '430 at col. 3, lines 63-68; see also Marko at pages 383-384. Note specifically that Little, at col. 3, lines 44-48, explicitly discloses that in a high concentration of chaotropic agent the silica-containing diatomaceous earth used therein preferentially binds larger DNA over RNA and small DNA linkers. Thus, each of the references differs from the claims only in that the claims recite a pH greater than 8 whereas the prior art uses a pH of 8.

However, keeping in mind the infinitesimally small difference between the claims and the prior art, the artisan of ordinary skill clearly would have had a reasonable expectation that pH values nominally great than 8 would have been useful in binding plasmid DNA to silica supports, based on the prior art's disclosure of the suitability of pH 8 in this type of process. Thus, the artisan of ordinary skill clearly would have been motivated to have used a pH greater than 8 in the processes disclosed by Little and Marko. Moreover, pH is well known to be a result-effective parameter routinely optimized in this type of

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process. Thus, the determination of a suitable pH range for plasmid binding clearly would have been an obvious matter of optimization on the part of the artisan of ordinary skill.

Claims 38-47 and 50-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (U.S. Pat. 5,075,430) and Marko et al (Anal. Biochem. 121(2):382-387 (1982) as applied to claims 38-42, 44-47, 50-53 and 57 above, and in further view of Smith et al (U.S. Pat. 6,027,945) and Segel (*Biochemical Calculations*, pp. 403-406 (Appendix IV), John Wiley & Sons, Inc., New York, 1976).

As discussed above, Little and Marko clearly render obvious Claims 38-42, 44-47, 50-53 and 57. However, neither of these references discloses the use of magnetic silica particles in the processes disclosed therein, as recited in claims 43 and 54. However, Smith clearly discloses the advantageousness of using such particles when purifying DNA by processes using chaotropic reagents. See, e.g., Abstract. Thus, the artisan of ordinary skill at the time of applicant's invention clearly would have been motivated by Smith's disclosure of the advantages of using magnetic silica particles to have used said particles in Little's or Marko's processes. A holding of obviousness over the cited claims is therefore clearly proper.

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Lastly, the substitution in claim 55 and 56 of a known buffer such as the amphoteric amino acid glycine (see, e.g. Segel at page 406) for the buffer used in Little or Marko must clearly be considered a substitution of one known buffer for a known equivalent, and therefore obvious under § 103(a).

Claims 48, 49 and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bastian et al (WO 95/21849 or U.S. Pat. 6,180,778 B1) in view of Segel (*Biochemical Calculations*, pp. 403-406 (Appendix IV), John Wiley & Sons, Inc., New York, 1976).

Bastian discloses solutions useful in purifying DNA, said solutions comprising chaotropic reagents (which may be thiocyanates), alcohols and buffers. See, e.g. discussion regarding lysis solutions at '778, col. 5, line 54 through col. 6, line 5; see also the various reagents disclosed by '778 at col. 7, line 59 through col. 8, line 18. Thus, the claims differ from the prior art in that the claims use a different chaotropic reagent than used in the prior art and a different buffer. However, the substitution of the known chaotropic agent, sodium thiocyanate, for the thiocyanate reagents in the Bastian references clearly must be considered the substitution of one known thiocyanate chaotropic agent for a known

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thiocyanate equivalent, and therefore obvious under § 103(a). Similarly, the substitution of a known buffer such as glycine (see, e.g. Segel at page 406) for the buffers used the Bastian references must clearly be considered a substitution of one known buffer for a known equivalent, and therefore obvious under § 103(a). Thus, absent a demonstration of something unexpected resulting from the use of these known equivalents, a holding of obviousness is required.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Francisco C Prats
Primary Examiner
Art Unit 1651

FCP
April 30, 2003